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EXAMINER	
LAM, ANN Y	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,783	SCHREIER ET AL.	
	Examiner	Art Unit	
	ANN Y. LAM	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 8-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Webster et al. 6,383,789, in view of Colman et al., 5,665,065, and further in view of Depeursinge 20030023345; or alternatively, over Webster et al., 6,383,789, in view of Price et al., 20010051635, and further in view of Colman et al., 5,665,065, and Depeursinge 20030023345.

Webster et al. teach that polymorphisms expressing a non-functioning variant enzyme results in a sub-group of patients in the population who are more prone to the concentration-dependent effects of a drug, and that genotyping allows identification of individuals who are prone to the concentration-dependent effects of a drug, thus permitting adjustment of the dose of drug to achieve improved therapy (col. 2, lines 39-54.). Webster et al. teach methods based in part on the identification of amino acid sequences of human drug-metabolizing enzyme peptides and proteins that are related to the UDP-glycosyltransferase drug-metabolizing enzyme subfamily, and allelic variants. Column 6, line 57 to column 7, line 12.

The proteins can be used in assays, to raise antibodies or to elicit another immune response, as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its binding partner or ligand) in biological fluids. Any or all of these uses are capable of being developed into reagent grade or kit format for commercialization as commercial products. Column 13, lines 44-61.

The drug-metabolizing enzyme proteins are also useful to provide a target for diagnosing a disease or predisposition to disease mediated by the peptide. Accordingly, the invention provides methods for detecting the presence, or levels of, the protein (or encoding mRNA) in a cell, tissue, or organism. The method involves contacting a biological sample with a compound capable of interacting with the drug-metabolizing enzyme protein such that the interaction can be detected. Such an assay can be provided in a single detection format or a multi-detection format such as an antibody chip array. Column 18, lines 8-21. One agent for detecting a protein in a sample is an antibody capable of selectively binding to protein. A biological sample includes tissues, cells and biological fluids isolated from a subject, as well as tissues, cells and fluids present within a subject. Column 18, lines 22-26. The peptides also provide targets for diagnosing active protein activity, disease, or predisposition to disease, in a patient having a variant peptide. Thus, the peptide can be isolated from a biological sample and assayed for the presence of a genetic mutation that results in aberrant peptide. This includes amino acid substitution, deletion, insertion, rearrangement, (as the result of aberrant splicing events), and inappropriate post-

translational modification. Analytic methods include altered electrophoretic mobility, altered tryptic peptide digest, altered drug-metabolizing enzyme activity in cell-based or cell-free assay, alteration in substrate or antibody-binding pattern, altered isoelectric point, direct amino acid sequencing, and any other of the known assay techniques useful for detecting mutations in a protein. Such an assay can be provided in a single detection format or a multi-detection format such as an antibody chip array. Column 18, lines 27-45. In vitro techniques for detection of peptide include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations and inumunofluorescence using a detection reagent, such as an antibody or protein binding agent. Particularly useful are methods that detect the allelic variant of a peptide expressed in a subject and methods which detect fragments of a peptide in a sample. Column 18, lines 46-58.

Webster et al. also disclose that the peptides are also useful in pharmacogenomic analysis. Pharmacogenomics deal with clinically significant hereditary variations in the response to drugs due to altered drug disposition and abnormal action in affected persons. The clinical outcomes of these variations result in severe toxicity of therapeutic drugs in certain individuals or therapeutic failure of drugs in certain individuals as a result of individual variation in metabolism. Thus, the genotype of the individual can determine the way a therapeutic compound acts on the body or the way the body metabolizes the compound. Further, the activity of drug metabolizing enzymes effects both the intensity and duration of drug action. Thus, the pharmacogenomics of the individual permit the selection of effective compounds and

effective dosages of such compounds for prophylactic or therapeutic treatment based on the individual's genotype. The discovery of genetic polymorphisms in some drug metabolizing enzymes has explained why some patients do not obtain the expected drug effects, show an exaggerated drug effect, or experience serious toxicity from standard drug dosages. Polymorphisms can be expressed in the phenotype of the extensive metabolizer and the phenotype of the poor metabolizer. Accordingly, genetic polymorphism may lead to allelic protein variants of the drug-metabolizing enzyme protein in which one or more of the drug-metabolizing enzyme functions in one population is different from those in another population. The peptides thus allow a target to ascertain a genetic predisposition that can affect treatment modality. Thus, in a ligand-based treatment, polymorphism may give rise to amino terminal extracellular domains and/or other substrate-binding regions that are more or less active in substrate binding, and drug-metabolizing enzyme activation. Accordingly, substrate dosage would necessarily be modified to maximize the therapeutic effect within a given population containing a polymorphism. As an alternative to genotyping, specific polymorphic peptides could be identified. Column 18, line 59 – column 19, line 30.

More specifically, Webster et al. disclose that the invention encompasses kits for using antibodies to detect the presence of a protein in a biological sample. The kit can comprise antibodies such as a labeled or labelable antibody and a compound or agent for detecting protein in a biological sample; means for determining the amount of protein in the sample; means for comparing the amount of protein in the sample with a

standard; and instructions for use. Such a kit can be supplied to detect a single protein or epitope or can be configured to detect one of a multitude of epitopes, such as in an antibody detection array. Arrays are described in detail below for nucleic acid arrays and similar methods have been developed for antibody arrays. Column 21, lines 52-63.

Webster et al. discuss in vitro techniques for detection of mRNA and DNA. Column 25, lines 57-60. Probes can be used as a part of a diagnostic test kit for identifying cells or tissues that express a drug-metabolizing enzyme protein, such as by measuring a level of a drug-metabolizing enzyme-encoding nucleic acid in a sample of cells from a subject e.g., mRNA or genomic DNA, or determining if a drug-metabolizing enzyme gene has been mutated. Column 25, line 61 to column 26, line 6. It is also disclosed that the nucleic acid molecules are also useful for monitoring the effectiveness of modulating compounds on the expression or activity of the drug-metabolizing enzyme gene in clinical trials or in a treatment regimen. Thus, the gene expression pattern can serve as a barometer for the continuing effectiveness of treatment with the compound, particularly with compounds to which a patient can develop resistance. The gene expression pattern can also serve as a marker indicative of a physiological response of the affected cells to the compound. Accordingly, such monitoring would allow either increased administration of the compound or the administration of alternative compounds to which the patient has not become resistant. Similarly, if the level of nucleic acid expression falls below a desirable level, administration of the compound could be commensurately decreased. Column 27, lines 3-17.

The nucleic acid molecules are also useful in diagnostic assays for qualitative changes in drug-metabolizing enzyme nucleic acid expression, and particularly in qualitative changes that lead to pathology. The nucleic acid molecules can be used to detect mutations in drug-metabolizing enzyme genes and gene expression products such as mRNA. The nucleic acid molecules can be used as hybridization probes to detect naturally occurring genetic mutations in the drug-metabolizing enzyme gene and thereby to determine whether a subject with the mutation is at risk for a disorder caused by the mutation. Mutations include deletion, addition, or substitution of one or more nucleotides in the gene, chromosomal rearrangement, such as inversion or transposition, modification of genomic DNA, such as aberrant methylation patterns or changes in gene copy number, such as amplification. Detection of a mutated form of the drug-metabolizing enzyme gene associated with a dysfunction provides a diagnostic tool for an active disease or susceptibility to disease when the disease results from overexpression, underexpression, or altered expression of a drug-metabolizing enzyme protein. Column 27, lines 18-38.

Webster et al. further disclosed that the invention also encompasses kits for detecting the presence of a drug-metabolizing enzyme nucleic acid in a biological sample. For example, the kit can comprise reagents such as a labeled or labelable nucleic acid or agent capable of detecting drug-metabolizing enzyme nucleic acid in a biological sample; means for determining the amount of drug-metabolizing enzyme nucleic acid in the sample; and means for comparing the amount of drug-metabolizing enzyme nucleic acid in the sample with a standard. The compound or agent can be

packaged in a suitable container. The kit can further comprise instructions for using the kit to detect drug-metabolizing enzyme protein mRNA or DNA. Column 29, lines 18-36.

The nucleic acid detection kits can be in the form of arrays or microarrays of nucleic acid molecules. The kits can contain the necessary reagents to carry out the assays. Column 29, lines 38-41.

Webster et al. specifically disclose providing a compartmentalized kit to receive, in close confinement, one or more containers which comprises: (a) a first container comprising one of the nucleic acid molecules that can bind to a fragment of the Human genome disclosed herein; and (b) one or more other containers comprising one or more of the following: wash reagents, reagents capable of detecting presence of a bound nucleic acid. Column 31, lines 36-43.

A compartmentalized kit includes any kit in which reagents are contained in separate containers. Such containers include small glass containers, plastic containers, strips of plastic, glass or paper, or arraying material such as silica. Such containers allows one to efficiently transfer reagents from one compartment to another compartment such that the samples and reagents are not cross-contaminated, and the agents or solutions of each container can be added in a quantitative fashion from one compartment to another. Such containers will include a container which will accept the test sample, a container which contains the nucleic acid probe, containers which contain wash reagents (such as phosphate buffered saline, Tris-buffers, etc.), and containers which contain the reagents used to detect the bound probe. One skilled in

the art will readily recognize that the drug-metabolizing enzyme gene can be routinely identified using the sequence information incorporated into one of the established kit formats which are well known in the art, if particularly expression arrays. Column 31, lines 44-64.

In summary, Webster et al. state that the disclosed uses are capable of being developed into reagent grade or kit format for commercialization as commercial products (column 13, lines 44-61), and that the kit can comprise the antibodies and other reagents needed to detect the target protein (col. 21, lines 52-63). Webster et al. give further details of a kit in regards to nucleic acid detection, specifically referring the necessary reagents, and/or arrays being packaged in a suitable container, and instructions in the kit for performing the detection (column 29, lines 18-41.) A kit can be compartmentalized to receive one or more containers which comprise a first container for one reagent and other containers for other reagents (column 31, lines 36-43.) The kit can include information for identifying the target analytes (column 31, lines 44-64.) A kit is equivalent to a “package” (as claimed by Applicant.) Moreover, Webster et al. teach that the reagents can comprise the materials necessary to diagnosing active protein activity, disease, or predisposition to a disease in a patient having a variant peptide (column 18, lines 46-58.) Webster et al. also disclose that the peptides are also useful in pharmacogenomic analysis of an individual to permit the selection of effective compounds and effective dosages of such compounds for prophylactive or therapeutic treatment. For example, in a ligand-based treatment, if a polymorphism is identified, substrate dosage would necessarily be modified to maximize the therapeutic effect

within a given population containing a polymorphism. As an alternative to genotyping, specific polymorphic peptides could be identified. Column 18, line 59 – column 19, line 30.

Thus, as to claim 8, the Webster et al. disclosure meets the limitation regarding a diagnostic indicator system for a patient-specific property that is relevant for the action, side effect, interaction, metabolism, absorption, distribution, metabolism, and elimination of a medicament, wherein the patient-specific property is a genetic property that is determined by gene expression testing, wherein the diagnostic indicator system is comprised of a detector or chip with at least one reactive substance that when reacted with a bodily fluid provides information regarding the physiological or pathological state of the patient, the dosage of the medicament, or both.

However, while Webster et al. teach a kit comprising containers and the necessary reagents and instructions for detecting drug-metabolizing enzyme nucleic acid expression, or the polymorphic peptides, Webster et al. do not disclose that the kit further comprises a drug. It is emphasized however that Webster et al. teach that the detection results can be used to adjust the dosage of a specific drug that an individual should receive. Webster et al. however do not disclose that the drug is also packaged in the kit with the detection materials.

However, the convenience or benefit of combining the drugs and a diagnostic assay apparatus in one kit or package is apparent to the skilled artisan as it is predictable that such a combination allows for the doctor or patient to perform a

diagnostic assay for determining the effective dosages of the drug, as discussed by Webster et al., and then to have readily at hand the drug to be administered.

Alternatively, such a combination of drugs and diagnostic materials in a kit is recognized by Price et al. While the drug and diagnostic material disclosed by Price et al. relates to viral, HIV infection or AIDS (paragraph 0052), the general concept of combining diagnostic and therapeutic materials in one kit would be understood by the skilled artisan (paragraph 0053 and 0054). It is disclosed in paragraph 0055 that in such kits, the diagnostic agents are preferably disposed within a distinct container of the kit. The combined therapeutic agents, however, may be combined within a single container of the kit, i.e., in the same composition as the flavopiridol compound, such as in a cocktail or admixture. They may alternatively be maintained separately from the flavopiridol compound, in a distinct container. In paragraph 0177, it is disclosed that the kits may also contain other pharmaceutically acceptable formulations, either for diagnosis/imaging or combined therapy. For example, such kits may contain any one or more of a range of anti-HIV drugs; non-specific anti-viral agents; anti-HIV antibodies and such like, as well as one or more diagnostics. In paragraph 0178, it is disclosed that the kits may have a single container (container means) that contains the flavopiridol or analog, with or without any additional components, or they may have distinct containers for each desired agent. Where combined therapeutics are provided, a single solution may be pre-mixed, either in a molar equivalent combination, or with one component in excess of the other. Alternatively, each of the flavopiridol or analog and other anti-HIV agent components of the kit may be maintained separately within

distinct containers prior to administration to a patient. In paragraph 0179, it is disclosed that the components of the kit can be provided in liquid or dry powder form.

The containers of the kit will generally include at least one vial, test tube, flask, bottle, syringe or other container means, into which the flavopiridol or analog, and any other desired agent, may be placed and, preferably, suitably aliquoted. Where separate components are included, the kit will also generally contain a second vial or other container into which these are placed, enabling the administration of separated designed doses. The kits may also comprise a second/third container means for containing a sterile, pharmaceutically acceptable buffer or other diluent. Paragraph 0180.

The kits may also contain a means by which to administer the flavopiridol or analog to an animal or patient, e.g., one or more needles or syringes, aerosols, inhalants or other such like apparatus, from which the formulation may be injected into the animal or applied to a diseased area of the body. The kits of the present invention will also typically include a means for containing the vials, or such like, and other component, in close confinement for commercial sale, such as, e.g., injection or blow-molded plastic containers into which the desired vials and other apparatus are placed and retained. [0181].

In sum, Price et al. disclose combining the drugs and diagnostic materials in a kit, and that the kit can have several containers as may be necessary. The skilled artisan would have recognized that providing both in a kit allows for the benefit of convenience. The skilled artisan would have recognized that such convenience would

also apply to the drugs and detection materials disclosed by Webster et al., that is, that such a combination would allow for the doctor or patient to perform a diagnostic assay for determining the effective dosages of the drug, as discussed by Webster et al., and then to have readily at hand the drug to be administered.

Applicant also recites in independent claim 8 "wherein the dosimeter and the diagnostic indicator system are interconnected and wherein the information regarding the dosage is supplied to the dosimeter for dispensing the medicament in accordance with the information regarding the dosage". It is noted that the claim read in light of the specification in paragraph 0014 is interpreted to mean that the interconnection is such that the information regarding dosage is supplied to the dosimeter without any action by the patient or physician. This however is not disclosed by Webster et al., nor Price et al.

However, the concept of combining a diagnostic device with a medicine dispenser is known in the art, as shown by Colman et al.

Colman et al. teach a medication infusion device comprising a compact programmable medication infusion pump adapted to receive and support a syringe carrying a prescribed medication such as insulin. The pump further includes a sensor or meter for detecting or receiving a current patient parameter, such as a blood glucose reading. The parameter sensor or meter provides a data input to the pump controller for altering the medication delivery protocol in an appropriate manner. In accordance with the invention, the altered protocol can be automatically implemented, but may in the alternative be recommended to the patient by means of the visual display for convenient

acceptance or rejection by manipulation of one or more of the control buttons, or otherwise overridden entirely by the patient in favor of a different or modified delivery protocol. See column 2, lines 46-64.

Colman et al. further teach that in an alternative embodiment, the medication infusion device comprises a manually operated syringe-type implement, such as a medication delivery pen. The delivery pen includes a manually adjustable dial or the like for retracting a syringe plunger through a predetermined stroke, in association with a visual display which indicates the medication dosage to be delivered. The delivery pen includes a controller which receives a patient parameter input from a sensor or meter, such as a current blood glucose reading. The controller responds to the data input representing the patient parameter to recommend a dispensing protocol which can be accepted or modified by the patient. See column 2, line 65 – col. 3, line 11. A glucose sensor or meter 16' such as a built-in sensor for receiving and reading a glucose test strip, provides a data input to the delivery pen 10'. An internal controller responds to the data input to provide a recommended medication dispensing protocol via the display 26'. The patient may operate the dial 42 and plunger 44 to deliver the recommended dosage. See column 5, lines 15-40.

Colman et al. further describes that a pump controller 24 responds to a data input from the glucose sensor or meter 16, in addition to manually inputted instructions by means of the buttons 22. The glucose sensor or meter 16 is conveniently mounted directly onto the pump housing 18 in a readily accessible position, depending upon the type of glucose sensor or meter used. See column 5, lines 41-60.

As to claim 8, the Colman et al. medicine dispenser is equivalent to the claimed dosimeter containing a medicament. The dosimeter, such as the delivery pen, is considered a chip, and it comprises a dispensing means to dispense the medicine. The Colman et al. sensor is equivalent to the claimed diagnostic indicator system comprising a detector, wherein the dosimeter and the diagnostic indicator system are interconnected and information regarding the dosage is supplied to the dosimeter for dispensing the medicament in accordance with the information regarding the dosage.

It is noted that while the exemplary embodiments disclosed by Colman et al. refer to the sensor as a glucose sensor, the disclosed invention is not limited to glucose sensing or infusion of insulin. This is repeated throughout the disclosure, in which the invention is disclosed generically and discloses blood glucose reading as an example for the sensor, and insulin as an example of medication. For instance, in column 2, lines 33-37, it is disclosed that the “improved medication infusion device includes data input pertaining to a current patient condition parameter, such as a current blood glucose reading, and responds thereto to provide an appropriate medication delivery protocol for the patient” (emphasis added). In column 3, lines 46-49, it is disclosed that “the medication infusion device comprises a compact programmable medication infusion pump adapted to receive and support a syringe carrying a prescribed medication such as insulin". In column 3, lines 6-11, it is disclosed that the invention may comprise a delivery pen in association with a visual display which indicates the medication dosage to be delivered upon subsequent plunger advancement, and that the "delivery pen includes a controller which receives a patient parameter input from a

sensor or meter, such as a current blood glucose reading". In column 3, lines 49-58, it is disclosed that in the exemplary drawings, a medication infusion device such as a programmable infusion pump is designed for programmable delivery of a selected medication such as insulin…."

Thus , the exemplary embodiments disclose a glucose sensor as the specific type of sensor, and it is understood that the invention is useful with regulating insulin delivery based on blood glucose level as well as other parameters since the improvement of the invention relates to the ability to enter other parameters that affect the medication requirement, such as current patient activity, eating schedules, etc., as would be desirable for determining the appropriate insulin delivery (col. 2, lines 37-45.) However, as shown above, it is understood that the invention is not limited to use for blood glucose level detection nor for delivery of insulin. Thus it is suggested that the invention can be modified to detect other desirable diagnostic indicators of a medical condition, and can be used to deliver the medicine appropriate for that medical condition. In any case, the skilled artisan would have recognized that the general teachings that can be derived from the teachings of Colman et al. regarding a combination device comprising a diagnostic device and medical delivery device can be applied to other medical conditions for the sample purpose, that is, to diagnose a particular condition and deliver the appropriate medicine in the appropriate dosage based on the diagnosis.

Moreover, while Colman et al. disclose as examples, an infusion pump or a syringe-type device such as a medication delivery pen, the skilled artisan would have

understood that various other means for delivering medicine can be programmed such that it delivers the appropriate dosage of medicine, as such is disclosed in the art, such as in the Depeursinge patent.

Depeursinge discloses a device including the following components: a pack wherein a pharmacist places at least one drug dose which was previously prepared by the pharmacist in the pharmacy, the pack thereupon being hermetically sealed and ultimately made available to the patient or some medical personnel; a storage substrate joined to the pack element and containing all patient identifying parameters, specific name, address, social security number etc., and the preparation of the prescribed drug: drug name(s), drug doses, time(s) of administration etc.; an initially locked programmed dispenser which can be manually or automatically unlocked to dispense one or more drug doses as a function of the parameters stored in the pack's storage; means identifying and reading the parameters and joined to the dispenser and activated when the dispenser is combined with the pack for the drug doses to be administered. Paragraph 0020-0024.

In one illustrative, and non-limiting embodiment, the pack and dispenser are particularly designed to contain drug doses in tablet form. Paragraph 0025. Such components may be modified to hold drugs in liquid, powder, or other forms. Paragraph 0026. In one embodiment, the pack consists of a container divided into a plurality of compartments each of which holds the previously loaded tablet(s) corresponding to a given drug dose to be ingested by the patient at a given time and at given time intervals. Paragraph 0027.

By means of a preset computer program, the dispenser's doors can be locked and unlocked in a selected sequence and as a function of the preset time intervals recorded in the storage substrate and managed by an electronic clock. Paragraph 0039. A button can drive a door to be opened to release the drugs. Paragraph 0042.

In paragraph 0049, it is also disclosed that the system is able to tell whether the corresponding door was opened. Detection is implemented by the processing unit based on the data recorded in the storage substrate, with on door-position data, provided by the switches, and with real time provided by an internal clock, illustratively a component of the processing unit. The detection may trigger an alarm to notify the patient of an omission in taking the drug.

Depeursinge discloses that the system allows supplying the drug in precise amounts (accurate drug dosages). Paragraph 0067. The system also avoids pateint errors. Paragraph 0006.

It is acknowledged that Depeursinge does not teach a diagnostic device nor interconnecting a diagnostic device with the drug dispenser such that the results from the diagnostic device would provide the information to the drug dispenser to controllably dispense an accurate drug dosage. It is emphasized however that this feature is disclosed in general by Colman et al., and Depeursinge is cited to show other types of drug dispensers that can be controlled by a processing unit. The skilled artisan would have recognized that interconnecting a diagnostic device with a drug dispenser, as derived from the teachings of Colman et al, can be provided in other types of drug

dispensers, such as the Depeursinge dispenser since it is controlled by a processing unit. Given the teachings of Colman et al., the skilled artisan would recognize that the processing unit controlling the drug dispenser disclosed by Depeursinge can be connected to a diagnostic device (sensor), as generally taught by Colman et al. for dispensing the appropriate drug dosage based on the diagnostic testing.

In summary, the prior art teaches the various elements of Applicant's invention, namely diagnosing a patient-specific property regarding the action, side effect, interaction, metabolism, absorption, distribution, metabolism, and elimination of a medicament, wherein the diagnosis provides information regarding dispensing of the appropriate dosage of the medicament (taught by Webster et al.) Administering the proper dosage of the medicament is also taught by Webster et al. Moreover, combining a diagnostic system with a therapeutic system in a package or kit can be readily apparent to the skilled artisan, or alternatively be suggested by the teachings of Price et al. The interconnection of a diagnostic system (sensor) with a medicine dispenser is also known in the art (taught by Colman et al.) Other types of medicine dispensers, such as that in tablet or liquid form that can be controlled by a processing unit is also known (taught by Depeursinge). The skilled artisan understands that the various known elements in the art can be combined, especially when it is desirable to do so for some benefit, whether suggested in the art or can be readily apparent or predictable by the skilled artisan. In this case, the convenience of providing a diagnostic system and therapeutic system in one package or kit is an apparent benefit, and is also suggested by Price et al. Interconnecting a diagnostic system with a therapeutic system for

controlling dosages of medicine based on the results of a testing performed by the diagnostic system, using for example a processing unit, also provides the benefit of convenience. Depeursinge also disclose that it provides the benefit of avoiding user error in implementing the dispensing of proper dosage. Thus the skilled artisan has ample motivations to combine the teachings to achieve the benefits disclosed by the references and that is readily apparent to the skilled artisan, namely for convenience of usage, and for avoiding user error. In short, the convenience and benefits of testing and automatic adjustment and metering of an appropriate dosage of medicine, using one device, is generally taught by Colman et al., and it is also disclosed by Colman et al. that such combination of elements not be limited to the specific diagnosis and treatment exemplified. The skilled artisan would have also recognized that such convenience and benefits can also be achieved where the detection allows for identification of individuals who are prone to the concentration-dependent effects of a drug, as disclosed by Webster et al., particularly when it is taught by Webster et al. that such detection allows for adjusting the dosage of a medication for improved therapy.

As to claims 9 and 14, Webster et al. teach that the diagnostic device can be in the form of arrays on a substrate such as paper, nylon or other type of membrane, filter, chip, glass slide (column 29, lines 42-46.)

As to claim 10, Webster et al. teach that in vitro techniques for detection of peptide include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations and inumunofluorescence using a detection reagent, such as an antibody or protein binding agent. Column 18, lines 46-58.

As to claim 11, a dispenser for individual dosing by a mechanical or electronic calibration of a liquid is disclosed by Colman et al. and of a solid or liquid is disclosed by Depeursinge as has been discussed above.

As to claim 12, the adjusted therapy is disclosed by Webster et al. in disclosing adjustment of dosage of the drug as discussed above.

As to claim 13, the device discussed above is capable of providing simple and unequivocal handling by the patient or nurse or physician.

As to claim 15, Webster et al. teach that detection of the genetic polymorphism can identify individuals that would not obtain the expected drug effects, or experience serious toxicity from standard drug dosages (column 18, line 59 – column 19, line 30) [i.e., a responder/non-responder property of an individual patient.]

Response to Arguments

Applicant's arguments have been fully considered but are not persuasive.

Applicant argues that Webster et al. do not teach a patient-specific treatment but a treatment based on a classification into a sub-group of population that is afflicted with polymorphism. Applicant emphasizes that the test of Webster et al. is performed only once, and that a general (statistical) and not an individually adjusted medication regime is then prescribed. Applicant notes that the present invention is directed to a more individualized approach, which allows for making available to the patient continuously the optimal dosage of the medicament, and allows a monitoring measuring unit that

continuously measures and documents the effect of a medicament and thus enables the patient or physician to continuously monitor the success or failure of a medication. Applicant argues that nothing suggests that according to Webster et al. that the genotyping procedure is employed routinely to determine the patient's condition and/or the response to the medication and to make adjustments throughout the therapy based on the analytical results.

In response, Examiner notes that nothing in the claims requires that the claimed apparatus be capable of continuous or repetitive diagnosis and metering of a medication. In other words, the claims read on an apparatus that allows for only a one-time diagnosis and metering. (It is noted that Graham et al., as cited in the "Conclusion" section below, discloses testing before and after administration of medication to monitor an individual's therapy to adjust the administration accordingly.)

Applicant's claimed invention appears to make convenient the ability to test, and automatically adjust and meter an appropriate dosage of medicine, using one device. Such general concepts are disclosed by Colman et al., and it is also disclosed by Colman et al. that such combination of elements not be limited to the specific diagnosis and treatment exemplified. The skilled artisan would have also recognized that such convenience can also be achieved where the detection allows for identification of individuals who are prone to the concentration-dependent effects of a drug, as disclosed by Webster et al., particularly when it is taught by Webster et al. that such detection allows for adjusting the dosage of a medication for improved therapy.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Graham et al, 6,287,805, discloses performing a diagnostic testing before and after administration of medication and monitoring the effectiveness of treatment based on the testing and altering administration of the medication accordingly. It is also disclosed that testing can be performed to identify an individual's drug response genotype. Column 47, line 14 to column 48, line 20.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANN Y. LAM whose telephone number is (571)272-0822. The examiner can normally be reached on Mon.-Thurs. 9-7:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ann Y. Lam/
Primary Examiner, Art Unit 1641